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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,688	01/07/2002	Yong Hua Zhu	LOMAU.143A	5449

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,688	ZHU ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/31/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10-12,14-18,20,22-24,26-29 and 31-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10-12,14-18,20,22-24,26-29 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 07/31/2006.

Claims 7, 9, 13, 19, 25 and 30 have been canceled.

Claims 1-6, 8, 10-12, 14-18, 20, 22-24, 26-29, 31-34 are pending and included in the prosecution.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-5, 8, 10-12, 14-17, 20, 23, 24, 26-29, 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/10374 ('374) in view of US 6,2143,352 ('352).

WO '374 discloses *in situ* polymerizing (*in situ* curing) biomedical implant material and a method for repair of mammalian tissue using the same biomedical material (abstract; page 8, line 35; page 9, line 1). The material comprises cyanoacrylate adhesive, hydrophilic porosifying agent and antibiotic (page 6, lines 9, 16-17; page 7, line 1; page 8, line 23 till page 9, line 2). The hydrophilic porosifying agent includes polyethylene glycol that dissolve *in situ* as a result of exposure to an aqueous environment, e.g. body fluids are aqueous (page 4, lines 20-23). The *in situ* polymerizing implant material is introduced into the repair site (reads on wound) by variety of means and is used as a sealant in anatomic regions where it would be difficult to use a pre-cast dressing (page 12, lines 12-19). Introducing the *in situ* polymerizing implant material into the repair site reads on the step of "approximating the wound" in claim 12. Polymerization *in situ* reads on the step of curing the adhesive in claim 12. The adhesive material is a liquid as implied by its application at the site by pouring (page 12, lines 12-15).

WO '374 does not teach encapsulating the active substance and materials of the capsules as claimed in claims 1, 12, 26 and 31. WO '374 does not teach butyl and octyl

cyanoacrylate as claimed in claims 2, 3, 14 and 15. WO '374 does not teach the anti-degradation agents claimed in claims 10, 11, 23 and 24.

Although the reference teaches that the porosifying agent dissolves in the aqueous environment, i.e. the body fluid, however, the reference does not teach the delivery of the substance to the tissue.

It is implied from the teaching of the reference that an active agent is delivered, such as anti-microbials including penicillin (page 12, lines 22-30). It is expected from the implanted composition that polymerizes *in situ* and comprises hydrophilic pore forming agent and active substance, to deliver the substance through the pores after the pore-forming agent dissolves.

US '352 teaches biocompatible cyanoacrylate adhesive comprises bioactive materials and other ingredients including pH modifiers are microencapsulated (col.4, lines 42-43; col.7, lines 60-65; col.8, lines 28-29, 35; col.10, lines 34-43). The microcapsules are made of bioerodible material to permits the release of the encapsulated material upon breakdown of the capsule in presence of body fluid (col.8, lines 18-26, 35). PH modifiers include materials that act as antimicrobials such as phenol compounds (col.6, lines 28-33). The reference disclosed that microencapsulation chemically protects the materials that interact with the adhesive and also provides controlled release of the bioactive agents (col.7, lines 41-43; col.10, lines 43-45). The preferred advantageous cyanoacrylates are butyl and 2-octyl cyanoacrylate (col.3, lines 3-6; col.17, claim 13). The pH modifiers are effective to regulate the pH of an immediate environment of the in situ formed polymer to improve the usefulness of

the polymers formed from the cyanoacrylate monomers and they are selected to permit the biodegradation of the in situ formed polymer to proceed more slowly than it does in physiological pH (col.2, lines 49-52; col.5, lines 38-44; col.6, lines 15-20). PH modifiers include ascorbic acid (col.6, line 49).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a composition and a method for sealing wound by applying adhesive composition comprising cyanoacrylate, pore forming agent and antibiotic as disclosed by WO '374, and encapsulated the antibiotics included in the composition in a gelatin capsule as taught by US '353, motivated by the teaching of US '352 that microencapsulation chemically protects the materials that interact with the adhesive and also provides controlled release of the bioactive agents, and one having ordinary skill in the art would have selected gelatin because US '352 disclosed it as a bioerodible material that breakdown in the presence of body fluid, with reasonable expectation of having adhesive wound sealing composition and comprises cyanoacrylate, pore forming agent and antibiotic encapsulated in gelatin capsule to chemically protect the materials that interact with the adhesive and breakdown in body fluid to provide controlled release of the antibiotics, as desired by applicants.

Additionally, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a composition and a method for sealing wound by applying adhesive composition comprising cyanoacrylate, pore forming agent and antibiotic as disclosed by WO '374, and select butyl or octyl cyanoacrylate as disclosed by US '352, motivated by the teaching of US '352 that butyl and octyl cyanoacrylates

are the preferred advantageous biocompatible cyanoacrylate adhesives, with reasonable expectation of having a biocompatible adhesive wound sealing composition comprises butyl or octyl cyanoacrylate, pore forming agent and antibiotic that is safe and does not cause any harm to the wounded tissues.

Further, one having ordinary skill in the art would have been motivated to add pH modifier such as ascorbic acid (vitamin C) disclosed by US '352 to the cyanoacrylate adhesive composition disclosed by WO '374, motivated by the teaching of US '352 that pH modifiers are effective to regulate the pH of an immediate environment of the in situ formed polymer to improve the usefulness of the polymers formed from the cyanoacrylate monomers and they are selected to permit the biodegradation of the in situ formed polymer to proceed more slowly than it does in physiological pH, with reasonable expectation of having adhesive wound sealing composition comprises butyl or octyl cyanoacrylate, pore forming agent, encapsulated antibiotic, and pH modifier such as ascorbic acid wherein the composition has delayed biodegradation of the in situ formed polymer and improved usefulness of the in situ formed polymer, as desired by applicants.

The combined teachings of the references do not teach specific antibiotics as claimed in claims 27-29 and 32 and 34. In any event, applicants failed to show superior and unexpected results that are achieved from using those specific antibiotics, and they do not impart patentability to the claims, absent evidence to the contrary.

4. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374 in view of US '352 and further in view of WO 96/00760 ('760).

The teachings of WO '374 in view of US '352 are discussed above.

However, WO '374 in view of US '352 do not teach the wound as a lacerated wound as in claim 22.

WO '760 teaches a biocompatible composition comprising pH modifier and butyl and octyl cyanoacrylate monomer wherein the composition is useful as biomedical and surgical adhesive and sealant that finds uses in repairing traumatically lacerated tissues, as claimed by present claim 22 (abstract; page 4, lines 6-12; page 5, line 17). In presence of blood, the composition has adequate flexibility and strength to withstand normal movement of the tissue and a bond strength that is maintained as natural tissue healing proceeds (page 6, lines 15-19; page 18, lines 23-32).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide composition and method for sealing the wound using adhesive composition comprising octyl or butyl cyanoacrylate, pore forming agent and encapsulated antibiotic as disclosed by WO '374 in view of US '352 and use the composition to treat lacerated wounds as disclosed by WO '760 motivated by the teaching of WO '760 that the cyanoacrylate composition finds uses in traumatically lacerated tissues because it has adequate flexibility and strength in presence of blood to withstand normal movement of the tissue and has a bond strength that is maintained as natural tissue healing proceeds, with reasonable expectation of having strong flexible wound sealant that comprises butyl or octyl cyanoacrylate, pore forming agent,

encapsulated antibiotic useful for traumatically lacerated wounds as it can withstand normal movement of the tissues and has a bond strength that is maintained as natural tissue healing proceeds.

5. Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374 in view US '352 and further in view of WO 99/20685 ('685).

The teachings of WO '374 in view of US '352 are discussed above.

However, the combined teachings of WO '374 in view of US '352 does not teach the molecular weight of the polyethylene glycol as claimed in claims 6 and 18.

WO '685 teaches a formulation that forms a film comprising water soluble pore forming agent such as polyethylene glycol that leaches out through the film *in situ* and creates a perforations that regulate the release rate of active agents (page 7, lines 10-16). The preferable molecular weight of the polyethylene glycol that is able to create adequate pore size for controlling the release of the active agents is from 540 to 8000, i.e. encompasses the molecular weight claimed by applicants in claims 6 and 18 (page 9, lines 23-28; page 10, lines 1-2).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide composition and method for sealing the wound wherein the composition comprises butyl or octyl cyanoacrylate, polyethylene glycol as pore forming agent and encapsulated antibiotics as disclosed by WO '374 in view of US '193 and select the molecular weight of the polyethylene glycol between 540 and 8000 as taught by WO '685 because this range of molecular weight is preferred because of

the ability of polyethylene glycol having such molecular weight to create adequate pore size for controlling the release of the active agents, with reasonable expectation of success of having wound sealant composition comprising butyl or octyl cyanoacrylate, polyethylene glycol with molecular weight ranging from 540 to 8000 as pore forming agent and encapsulated antibiotics wherein the polyethylene glycol creates pores of adequate sizes for controlling the release of antibiotics to the treated wound.

Response to Arguments

6. Applicant's arguments with respect to claims 1-6, 10-12, 14-18, 20, 22-24, 26-29, 31-34 have been considered but are moot in view of the new ground(s) of rejection.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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